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Overview
Help | FAQ
Tutorial
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
LinkOut
Cubby

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Order Documents
NLM Catalog
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

The ARO4 gene of Candida albicans encodes a tyrosine-sensitive DAHP synthase: evolution, functional conservation and phenoty Aro3p-, Aro4p-deficient mutants.

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The enzyme 3-deoxy-D-arabinoheptulosonate-7-phosphate (DAHP) synthase catalyses the first step in aromatic amino acid biosynthesis in prokaryotes, pl fungi. Cells of Saccharomyces cerevisiae contain two catalytically redundant synthases, encoded by the genes ARO3 and ARO4, whose activities are feed inhibited by phenylalanine and tyrosine, respectively. ARO3/4 gene transcrip controlled by GCN4. The authors previously cloned an ARO3 gene orthologi Candida albicans and found that: (1) it can complement an aro3 aro4 double in S. cerevisiae, an effect inhibited by excess phenylalanine, and (2) a homoz aro3-deletion mutant of C. albicans is phenotypically Aro(+), suggesting the of another isozyme(s). They now report the identification and functional characterization of the C. albicans orthologue of S. cerevisiae Aro4p. The twenzymes share 68% amino acid identity. Phylogenetic analysis places the fur DAHP synthases in a cluster separate from prokaryotic orthologues and sugg ARO3 and ARO4 arose from a single gene via a gene duplication event early fungal evolution. C. albicans ARO4 mRNA is elevated upon amino acid star consistent with the presence of three putative Gcn4p-responsive elements (G the gene promoter sequence. C. albicans ARO4 complements an aro3 aro4 do mutation in S. cerevisiae, an effect inhibited by excess tyrosine. The authors engineered Deltaaro3/Deltaaro3 Deltaaro4/MET3p::ARO4 cells of C. albicar one wild-type copy of ARO4 placed under control of the repressible MET3 p and found that they fail to grow in the absence of aromatic amino acids when expression is repressed, and that this growth defect can be partially rescued b aromatic amino acids and certain aromatic amino acid pathway intermediates concluded that, like S. cerevisiae, C. albicans contains two DAHP synthases for the first step in the aromatic amino acid biosynthetic pathway.

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